

Olden, Kenneth 2009

Dr. Kenneth Olden Oral History 2009

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NCI Laboratory of Molecular Biology Oral History Project

Interview with Dr. Kenneth Olden Conducted on January 13, 2009, by Jason Gart

JG: My name is Jason Gart and I am a senior historian at History Associates Incorporated in Rockville, Maryland. Today's date is January 13, 2009, and we are talking via telephone. I am in my offices in Rockville, Maryland, and I am speaking with Dr. Kenneth Olden.

Please state your full name and also spell it.

KO: Kenneth Olden. That is K-E-N-N-E-T-H—O-L-D-E-N.

JG: Terrific. Where are you located this morning?

KO: I am in my office at the School of Public Health at Hunter College in the City University of New York. That is on East 25th Street in the Brookdale Campus.

JG: Terrific, thank you. Established in 1970, the Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, commonly known as LMB, currently has among its ten groups four members of the National Academy of Sciences. LMB has trained many other prominent scientists and its research has contributed both to the basic science and to novel applied cancer treatments. LMB has initiated this oral history project to capture recollections of prominent scientists currently and formerly associated with the laboratory. You were born in July 1938 in Tennessee?

KO: Yes.

JG: Talk about your interests as a child.

KO: Well, I was always interested in reading and I read from cover to cover almost all the books that I could find around my home. However, the reading materials were limited because my dad was a farmer and he finished the eighth grade and my mother finished a third year of high school. We did not have a lot of books around but I enjoyed reading and so I read books. As a matter of fact, one of the books I was most familiar with was the Bible, and maybe not from so much a religious perspective, but it was a book, and I learned and I grew. I was always interested in growth intellectually and reading and that was maybe unusual for a farm boy because the emphasis is on physical activities that are required for farming because farming is heavy lifting.

JG: You mentioned your parents; did you have siblings?

KO: Yes, I had three sisters and one brother. We all grew up together on the farm and we helped with the chores. Those were responsibilities that we had and I learned the value of hard work and independence. In other words, make your own way through life and to be self-reliant.

JG: I read that the local school system was segregated at that time?

KO: That's right. Integration in the public school system in Tennessee did not happen until long after I had graduated from high school. The universities integrated after I graduated from college, in fact. The University of Tennessee actually integrated the undergraduate school in 1961. I graduated in 1960. I could not go to the University of Tennessee for college. I went to Knoxville College, which is in Knoxville [Tennessee], where the University of Tennessee is mainly located. The medical school is in Memphis but I went to school in Knoxville. I did during my senior year in college attend a research course at the University of Tennessee that was sponsored by the University of Tennessee and Oakridge National Laboratory. I became interested in research because of that experience and decided that I wanted to get a Ph.D. in biomedical research in some area of medicine. I was going to medical school prior to that.

JG: Let's go back for a moment to your childhood years. Talk about some of your mentors and how you were able to go from the farm to college.

KO: Right. Well, when I went to high school I had a high school principal who was from Knoxville, Tennessee, and he drove up to Newport on a weekly basis and he encouraged us. Most of the other teachers did not encourage me or any of the other kids to go to college because I guess the expectation was that we would become farmers or take other jobs that were available to blacks in the 1950's. I went to high school in Newport, Tennessee, which was about six or seven miles from the farm town [Parrottsville] that I grew up in because there was no high school. We rode a bus six or seven miles in one direction every day.

Most of the people in that community did not go to college, period. In my class I think there were two of us who went to senior college and one of us that went to a junior college. That was atypical; most people did not. They grew up and they took menial labor jobs which were about the only kinds of jobs that were available to anybody, black or white, at that time in Parrottsville or Newport. Particularly for black kids, there was nothing to do because there were only two or three industries there at the time. So it was working in gas stations, farming and janitorial work at the time. Many people actually left the area and, matter of fact, all my brothers and sisters migrated out to New York, Detroit, and Florida, someplace looking for opportunities.

The principal encouraged all of us to go to college. He emphasized intellectual pursuits and he said, "You can be anything you want." Most of the kids did not pay any attention to him because they never believed him, because they did not see role models in their community. I did, and I do not know for what reason, but I did, and I worked hard in high school to get good grades because I wanted to go to college and I got grades good enough to get into Knoxville College. For money, I worked after school. Once I got to high school then I did not work on the farm anymore. About that time my dad gave up farming and took a job with the U.S. Postal Service. We had chores after we got home but not daily farming.

I shined shoes at a barber shop downtown in Newport, Tennessee, for fifteen cents per pair and I was able to save enough money to put myself through college the first year. I set my money aside because I knew I wanted to go to college. However, I was fortunate to get a scholarship. My principal was instrumental in helping to arrange for me to go to Knoxville College and he also arranged through Knoxville College, for me to go with other students to Wildwood, New Jersey, to work in the summer in the tourist industry. I guess I was seventeen at the time. I went to Knoxville and joined a group of students and we traveled by bus to Wildwood, New Jersey. I worked there for several summers actually. I was able to make enough money every summer to pay my tuition and room and board in college. That is how I got through school.

JG: You entered Knoxville College in 1956?

KO: Yes.

JG: What were your aspirations? What did you see yourself doing after college?

KO: Role models play an important role and there were not many black professionals in my community. There were school teachers and there was one black physician. There were preachers and other people who were, in a sense, middle class but the middle class population was small and limited because of opportunities. I decided teaching did not interest me and being a minister did not. I decided I wanted to be a physician. There was a black physician in the community and so I decided to go to medical school. I was a pre-med major in college which means I majored in biology and minored in chemistry. I was a good student. I worked very, very hard. I guess I could count all my dates in college on the fingers of both hands and have fingers left. I just did not have time for those kinds of things. I was determined to succeed no matter. I was going to work hard enough to succeed.

It turns out the education that we got in little towns like Newport and Parrottsville was not very good. Even though Knoxville College, on a national scale, was not that competitive, for me it was, and I found it very difficult to make good grades. But I was determined to do so. I am not sure I made the Dean's List my first year, but I did pretty much from then on. I made A's and B's. I was going to go to medical school until I went to the University of Tennessee and participated in a research course my senior year in college. It was that experience though that taught me that this was fun. I really enjoyed research even though there still were no role models—African Americans.

I decided that was one thing that I could do to make a contribution to society at large, and certainly to the African American community, by getting a Ph.D. in the biological sciences and medical sciences and become nationally competitive and visible. That would be something that other youngsters could look to. It would be a statement that you can achieve and be productive in science irrespective of your race or your background if you work hard enough. So I decided to go get a Ph.D. in biological sciences and that was the best decision I ever made. It was the right decision for me and I enjoy science and I have been able to make important contributions, I think, to society and I was able to become nationally competitive and highly visible and that makes a difference.

Just last night, Medgar Evers College in Brooklyn hosted a reception for me to welcome me to New York City. The receptivity and the joy of the African Americans in that room . . . Medgar Evers College in Brooklyn, even though it is in New York, it is predominantly an African American institution. There were about seventy-five people there at the reception and the attendees were obviously pleased to see someone introduced like me with my skin color, my background as the Founding Dean of the School of Public Health here at the City University. They obviously took great pride in my background and my academic track record. They took great pride in that. They made it clear. The president of Medgar Evers College, who happens to be an African American, reports to the chancellor of the City University of New York, who happens to be a Caucasian, and the president made it very clear to the chancellor that my appointment was a source of great pride to that community and to that institution. They were especially pleased that the chancellor did that.

I always wanted to make a difference even when I was back on the farm. I wanted to do something to make a difference for people like my parents and my friends, my relatives, and other poor people, black and white, who grew up in my community. Poverty is a condition. It is an issue that we do not take seriously enough and when we do we tend to think that only racial ethnic minorities are poor but whites are poor as well and they do not have a chance either. Somebody has got to represent that group and I have made it my life ambition to be a spokesperson for the poor and the socioeconomically disadvantaged populations because I have not forgotten what it was like to be disadvantaged.

JG: You graduate from Knoxville College in 1960?

KO: Yes.

JG: You got a master of science degree from the University of Michigan in 1964?

KO: Yes. Well, I did not have mentors. I did not have anybody to go to and say "How do you do this." I did everything on my own and fortunately I made it but I made mistakes along the way. The mistake was I did not know that a master's degree would not allow me to do what I wanted to do. I went to get a master's degree and part of the time I had to work. I had to take off from Michigan to work. The point is if I had known what I do today and I would have gone straight into a Ph.D. program. After finishing the master's program I came here to New York to work.

JG: Where did you work?

KO: Columbia [University]. The College of Physicians & Surgeons in the Biochemistry Department. It turns out that I worked for an assistant professor in biochemistry who was a really wonderful fellow and he became a mentor.

JG: This is Dwayne Price?

KO: Yes, Dwayne Price, and Dr. Price recognized that I had ability and he encouraged me to go back to get my doctorate and I guess I worked for him a year, not long, and I did go back to Temple University to get my Ph.D.

JG: When you were in the biochemistry department and even at the University of Michigan what were your scientific interests? What were some of the things you were working on and what was the state of science in that period?

KO: Genetics was still *Drosophila*, and counting corn kernels, and it was mostly at the level of the chromosome, fruit flies, and I developed an interest in genetics. I must admit though that I have always been a kind of renaissance person. I can never learn too much. I am inquisitive and I like learning. I enjoyed all my courses at Michigan. Michigan had a policy in those days—I was in the zoology department—they wanted you to be very broadly educated. They wanted you to take courses in genetics, developmental biology, microbiology, entomology, and I liked that. You had to take something called a "cognitive" and that is something biologically related but outside of biology. I took a course called physical anthropology. I really enjoyed all those courses. Now I say to my wife and children that I can appreciate the environment in a way that I think a lot of people can't because I understand the source and meaning of the chirping sounds at night and all the insects and the things they do. I am still that way but that was before molecular genetics and molecular biology wasn't so strong. When I went back to get my Ph.D. certainly cell biology was becoming in vogue and molecular biology. I developed an interest in cell biology and my emphasis at Temple was cell biology and biochemistry.

JG: Did you consider going back to the University of Michigan?

KO: No, I did not. I was already on the East Coast and when I was at Michigan my research was in *Drosophila* genetics. When I got out here I wanted to stay on the East Coast. Well it turns out that I went to Temple to work with a person in *Drosophila* genetics. There was a fellow at Temple—Ralph Hillman, H-I-L-L-M-A-N, and Dr. Hillman had worked with Theodosius Dobzhansky. Dobzhansky was a famous geneticist at Columbia. The person I worked with at Michigan was also a student of Dobzhansky and I felt that I could get the same knowledge and training under Hillman in the same system as I did at Michigan and I would be on the East Coast. I decided to do that but it turned out that after I got to Temple my interests in genetics, and particularly the kind of work that Hillman was doing at the time, did not interest me as much as some of the new areas in cell and molecular biology.

JG: In what ways?

KO: Hillman's work was still more at the chromosomal level. Temple at that point recruited, in particular, two very interesting young faculty members. They brought in a fellow from Yale [University] named Harry Rappaport. Well, they brought in three. Another guy named Joseph Elon and finally the person I ended up working with named Walter P. Hempfling. Rappaport and Elon were molecular biologists, and Hempfling, whom I worked with, was a cell biologist. He was interested in oxidative phosphorylation mechanisms and things like that. I decided to work in that area and that is where I concentrated my effort and that required a fair knowledge of biochemistry. I took biochemistry and cell biology and did my thesis work in bioenergetics, oxidative phosphorylation area.

That worked for me because when I finished qualifying exams in foreign languages and cell biology for my Ph.D., Hempfling moved to become an associate professor at the University of Rochester and I went with him. I had met the requirements at Temple and so my degree is from Temple but I spent two years at Rochester. While at Rochester, when I was finishing up my Ph.D. thesis work, I realized that there were medical applications. I understood the connection between how cells utilize and expend energy to do things. There was a fellow at Harvard Medical School, named Tom Wilson, who worked on membrane transport. Membrane transport was a real big deal in those days, especially the mechanism of energy coupling. In other words, what was the source of energy and how was it coupled to move a molecule across a membrane. I decided that I did not want to do straight oxidative phosphorylation type of research, but I wanted to apply it to understand biological process such as transport. I applied to do a postdoc with Dr. Wilson in the physiology department at Harvard. Dr. Wilson invited me up for an interview, and to make a long story short, he offered me the position and that was a really good experience.

While at Harvard I stayed four and a half years and could have stayed longer because I had my own faculty fellowship. I was first a NIH postdoc, but toward the end of my third year, I got a Macy's Faculty Fellowship, and the Macy's Faculty Fellowship supported me for the rest of my time at Harvard. I had my own support then and so I moved out of Wilson's laboratory to a semi-independent position as an instructor. I worked with two faculty members: Fred Goldberg who is still there. He is a full professor and he works on protein degradation. Fred and I did some interesting work on mechanism energy coupling for protein degradation. Our work turned out to be a very novel and interesting contribution and when the Nobel Prize was awarded to the Israeli group lead by [Avram] Herskko for working out the mechanisms of protein degradation one of the seminal discoveries that was cited—I guess it was a *Nature* paper about the Nobel Prize—were our findings, demonstrating that the source of energy for protein degradation is ATP and it is absolutely required. In other words protomotive force is not adequate. You have got to have an ATP and split that bond and we demonstrated that. That was the first really exciting and mainstream discovery that I made.

I also worked with Eugene Kennedy. Eugene Kennedy was a professor and chair of biochemistry at Harvard and he and I had a sidebar conversation after a seminar one day and based on that conversation we decided to do an experiment together. We did an experiment where we demonstrated—again it had to do with energy coupling—that you could generate the vesicles from bacteria membranes or *E. coli* by sonification of the cells that were generated about fifty percent as right side out vesicles and fifty percent inside out. He and I were interested in how one could isolate those two classes of vesicles.

Kennedy and I figured out how to separate those two classes of vesicles because the ATPase was on the inner or cytoplasmic surface, so we did an affinity purification using antibodies to ATPase. That again turned out to be a very nice paper. Leon A. Heppel, the fellow at Cornell who gave the seminar, he kept bemoaning the fact that we could not do certain kinds of experiments because of this mixed population of vesicles. After the seminar, I went to Kennedy and said maybe I missed something but it seems to me that we could separate the two populations of vesicles using antibodies to the ATPase and affinity chromatography. He agreed and we did it. We published that paper together in PNAS [*Proceedings of the National Academy of Sciences*]. The person, a postdoc at the time, who actually did the work was named James Hare and he is now out in Oregon I think. I just saw him within the last two years. It was my idea, and Kennedy and I worked out the protocol, and it turned out to be a nice piece of work.

JG: You have benefited from working at several academic institutions. What was the difference between Harvard, Temple, the University of Rochester, and Michigan?

KO: I learned probably the most critical lesson of my career at Harvard and it continued in Ira Pastan's lab. At Harvard they want to train people who are going to be at the top of their field. They are not interested in somebody who is just going to be a plodder and somebody who is just going to be average or whatever. They wanted to create leaders and you got the impression . . . They would say to you, "Ken, you can work fourteen and fifteen hours a day on something of little interest, or you can spend that time working on something *really* important." If you are going to spend fourteen to sixteen hours a day why not just work on something important that is cutting edge and at the front. You lead the field. I learned that. Now there are risks of doing that because there is no road map and you are not just confirming or extending somebody else's work. You are writing the road map. Other people are going to come behind you and they are going to either replicate or not replicate or disagree with you and you have to formulate models without a lot of indicators based on your instincts.

I learned to go after research questions that if I succeed in answering them people are going to pay attention. If I write a paper, people are going to read it. I always focus on trying to identify where is the jugular vein here? What is really important? Of all the questions you can ask, here are ten questions, but which one is really important that people are going to take notice of? I learned this valuable lesson working at Harvard and by working with Ira Pastan. I was back at Harvard recently as a visiting professor in the School of Public Health in 2006-2007 and it is still that way. They are in the business of creating leaders. There are certain places that do that and that is what they want. I spent four and a half years at Harvard as an NIH Postdoctoral Fellow and a Macy Faculty Fellow, but Harvard set my salary and by that point I was married and I had three children. The salary was so low that I could not afford to stay any longer.

JG: I read that you and your wife ran a dormitory at Radcliffe College.

KO: Yes, that's right. Even though that was a good break for us, the money that we made . . . We had three kids and we were clothing them mostly on our credit cards at Sears and Penney's [J. C. Penney Company]. We decided to go someplace else where I could earn a better income but also do science in a group every bit as good as the one that I was in at Harvard. Ira Pastan had been offered the chair of the Physiology Department at Harvard when I was there, and I knew that, and I had been to a couple of his lectures when he came through to give talks. His lab was every bit as good. He was every bit as good as anybody I worked with at Harvard.

JG: What were your impressions of NIH when you were at Harvard?

KO: Very good. It turns out that in the old days everybody went through the NIH. If you were going to make it in science you went through the NIH. Now that turned out that that wasn't quite true because people went to NIH to get out of the Korean War and Vietnam. But when I walked through the parking lot of the medical school at Harvard you saw old NIH parking stickers on the old cars.

JG: Did you really?

KO: Yes. I would say most people in those days went through the NIH and if you take people like Harold Varmus, he went through the NIH. Just everybody went through the NIH and so I felt that NIH was every bit as good as Harvard and I still think it is. So I can go there. It turns out I did not know much about animal cells and tissue culture and I wanted to change directions a bit. I was working in bacterial systems at Harvard although answering questions relevant to humans, but I wanted to actually work with mammalian systems and Ira Pastan was putting together a group of people to do that. I was one of the first core members of that group.

JG: Were you recruited by Ira or did you call him up?

KO: I knew him so I wrote him a letter and told him who I was and that I was interested in his lab and for what reasons and so forth. I had three or four people from Harvard who knew me to send him a letter on my behalf. Ira invited me down to give a seminar and for an interview. He notified me while I was there that he wanted to take me and offered me a position. It was in large part based on some of the letters that he received.

There was one fellow I remember named Bernard Davis. Bernard Davis was a very eminent professor and he was a microbial geneticist and he was one of three people that probably should have received the Nobel Prize with [George W.] Beadle and [Edward L.] Tatum and that was what everybody said. Somehow Bernie did not but he had done work comparable and was one of the major contributors to microbial geneticists and many people thought he should have shared the Nobel Prize with Beadle and Tatum. He was certainly a leading scientist, a member in the National Academy of Sciences, and he wrote a very short letter for me, a paragraph or so, but it was powerful. Bernard Davis was not . . . I had never worked with him but he was a person that I knew I should get to know. He in fact was someone I needed to consult with during my research in Tom Wilson's laboratory so I did.

What was ironic about that was that Bernard Davis had a reputation of being a racist. Most blacks would not say hello to Bernie and because . . . I don't think that was true at all but the point is he got his name associated with another couple of social scientists— [Richard J.] Herrnstein and [Arthur] Jensen. Herrnstein and Jensen had some theories, something like the bell shaped curve, and Bernie somehow got associated with that and so there was that issue. Yet Bernie wrote a very strong letter for me and he knew I was African American because we talked together a lot of times. He had invited me to have lunch with him many times at the faculty club. He believed in my intellectual capacity and that I was going to be a major contributor. The fact that he wrote a letter for me got Ira Pastan's attention because Ira knew his reputation. I had others. Eugene Kennedy at that time was a member in the National Academy of Sciences and was a distinguished professor at Harvard. I had a lot of high powered people who believed in me and supported me. Bernard Davis turned out to be a mentor of mine. If you look at my publications even after I came to the NIH, he supported many of the papers that I got published in the *Proceedings of the National Academy of Sciences*. In those days a member had to communicate your paper otherwise you could not publish it. Bernard Davis signed off on mine and his name is on them.

JG: How did Ira describe what the lab was doing? What were the aspirations of Ira's lab when you arrived?

KO: Ira had one of the most exciting groups of people. He brought in myself, Ken Yamada, there was a fellow named Mark Willingham there in those days. All of us had some overlapping skills but he probably put together one of the first interdisciplinary research teams. He put us all in one corridor basically and there was a ferment there and interactions. Ira did not do experiments with his own hands but he walked up and down the hall and talked to us about our work and he was there every day. He went on vacation for one month (in July) but he called in almost everyday so we had direct access to Ira and he was a member of the National Academy of Sciences. You also had somebody working back-to-back with you at the bench. Ken Yamada from Stanford, and top people, just some of the best young scientists in the field.

I shared a lab with a fellow named Jacques Pouysegeur from France and Jacques had done very, very well. He is one of the most highly regarded French scientists even today. The three of us shared a laboratory. Both Ken and Jacques went on to make important contributions in science. We were just buddies and a team. The other thing that Ira did was he promoted collaborations. In other words, I would do what I knew how to do best, Ken would do what he knew how to do best, and Jacques, or somebody else, would do something else. We would get together and go over the data, plan the experiment and execute them, and publish them. Ira, like Harvard, understood competition. To have an idea is one thing, but to generate the data to support a hypothesis, is what it is about and getting it published before others. Being first is important. That was Harvard's view and that was the NIH view. Ira Pastan's view let's say.

JG: Describe Ira Pastan? Was Max Gottesman there at the time?

KO: Yes, Max Gottesman was there.

JG: Bob Perlman, was he there?

KO: Bob was not there but Bob Perlman was one of the people I knew at Harvard. He was in the physiology department and so Bob was another person who spoke to Ira on my behalf because they had worked together many, many years. That was how I got in.

JG: What type of scientists are they? Describe them.

KO: Well, let me say Ira was—and I guess he still is—very, very pushy. You had to work like hell. The way he did it, of course, is that he had weekly lab meetings and every week you had to get up and present something or say, “I didn’t do anything this week.” You did not want to do that. He had a way of forcing you to work and then he was always there. Even on the weekends he would often come around, Saturdays certainly. You never knew when he was going to come in. He did not spend the whole Saturday there, at this point, you know, he was an Academy member, but he would walk through the lab, the corridor, up and down, and say “hello” and see who was there. If you were doing an experiment you would have a chance to chat with him. You knew he was going to do that and you figured I want to be well received and thought of as somebody who works hard and does his best. So I worked Saturdays and Sundays. In hindsight I am sure Ira did it because he knew that we didn’t want him to walk through the lab many times and not see us on Saturdays and Sundays. We got a lot of work done. I was very productive during my time in his lab. I think I produced four good manuscripts per year in top journals and that is not bad.

JG: What type of research were you doing at this point?

KO: I went there as a senior staff fellow which is about equivalent to an assistant professorship in a university. When I left Harvard to come to Ira’s group I was being offered assistant professorships in good universities, for example, the University of Michigan offered me assistant professorship in the physiology department and other places were offering me assistant professorships. I decided that I did not want to do that. I wanted to come into a group that would allow me to change research directions. At that time, senior staff fellowships, or fellows, were not tenured and they were not tenure track. I was willing to come and work in Ira’s group because I liked what he was doing and I had thought tenure did not mean anything if you were productive and I intended to be productive. I worked on membrane proteins. That is what Ira was working on in animal cells. He was interested in membrane protein and so my first research and first few publications were looking at the association of myosin to membranes in animal cells.

Ken Yamada and I were in this same group. Ken and Ira worked on this protein called fibronectin and turns out that I read a paper by George Palade, and George Palade had won the Nobel Prize for how cells secrete proteins. In George Palade’s Nobel Prize paper—you always write a paper someplace—and I think he wrote his in the *Journal of Cell Biology*. Anyway in the paper that he wrote he summarized his views about protein secretion. He proposed or postulated that carbohydrates on proteins that are exported or secreted from the cell serve as a destination marker. Carbohydrate groups directed proteins to be secreted. In other words, it served as the zip code. While the evidence for this was indirect, it became dogma.

JG: This became canon.

KO: Yes, it became dogma. I looked at the data. If you list all the proteins that are exported, not all of them had carbohydrates attached to them and the most obvious one is albumin. You could argue that maybe albumin had the carbohydrate group on it earlier that got it into this export system and then the carbohydrate was cleaved off. Well it turned out that was not the case. Albumin does not even have the amino acid residues to allow for glycosylation. I concluded that it was just an hypothesis and his proposal was not right.

I set out to prove it and since fibronectin is a glycoprotein with five glycosylation sites, I decided to use it as a model to investigate the question. It turns out that a fellow in Japan named Tamura had discovered a chemical that could block glycosylation of n-linked glycoproteins. Fibronectin is a major extracellular protein. Five percent of the total cell protein. I said, “Wow, you can’t miss that.” If I prevented the glycosylation of it can it get secreted? According to Palade’s model it should not. When we blocked the glycosylation it still could get secreted, but it turns out it was not easy to interpret the results because when you block the glycosylation of the protein it got degraded fast. You altered the conformational structure and it gets degraded so you could be tricked because you look into the cell membrane, or into the medium, and the amount of the protein went way down so you said, “Yes, he is right.” That is what people had seen.

When we analyzed the cells more closely we could see that fibronectin accumulated in the endoplasmic reticulum. When we added inhibitors of proteases, suddenly you could get more of the unglycosylated protein on the membrane and in the medium. We concluded that it was not that carbohydrate groups were required for secretion but in some cases it was required to stabilize the structure of the protein. If a protein's tertiary confirmation gets distorted proteases will chop it up. This is something I knew from my work on protein degradation when I was at Harvard with Alfred Goldberg.

This published work turned out to be a seminal paper. It became one of the most highly cited papers in 1978 and when we published it in *Cell* demonstrating that you did not need a carbohydrate group on proteins. We focused primarily on fibronectin and collagen which are two major glycoproteins and we proved unequivocally that carbohydrates are not needed for secretion. This publication changed the dogma. It disproved the dogma. I remember when Ira and I were writing the paper, I came up with a title that was kind of weak. Ira said to me, "Do you believe your work?" I said yes. He said, "Well, why don't we be aggressive, be bold about it?" Let's say carbohydrate group is not required for secretion of glycoprotein and that is the title that came out in *Cell*. We said it is absolutely and unequivocally not required. Of course, that went against the dogma and the reviewers at *Cell* made us put every nail in the coffin to really debunk the established view and we did. The results were rigorous and definitive and that is why the paper became one of the most highly cited papers that year.

I submitted the abstract to the Cell Biology Meeting and George Palade was very active in the Society in those days. He showed up, to hear my presentation. It was in a large room and there was standing room only because it was exciting. My title was "Carbohydrate Groups Are Not Required for Secretion of Glycoproteins." Everybody wanted to see the data that I had. After my presentation there were questions, George Palade came up and congratulated me. We had done it. We nailed it, and this is again an example of why it is important to work on interesting problems. We were the first; we were not second or third.

There was one lab in particular at the University of Washington that published a paper right about the same time saying carbohydrate groups were required. He was using collagen, the same molecule that we used, but he made the mistake about the proteases, the degradation part. What he saw was a decrease in collagen secretion, but he never discovered and he didn't see aggregation in the endoplasmic reticulum and degradation. This guy was very famous. It took a lot of courage for us to go against the dogma. I learned to be courageous in science like in every other thing. When you are out front, the first to say it, everybody is going to check it. It has been checked time and time and time again. In fact we now know that it is a primary sequence of proteins that serve as the signal for protein secretion. Günter Blobel eventually got a Nobel Prize for identifying the secretory signal.

JG: Your first stint with NIH, you stay through 1979?

KO: Right.

JG: Then you go to Howard University?

KO: Right.

JG: During that first period how did you grow as a scientist?

KO: I would say that of all the decisions I made going to Harvard was an important one but the most significant decision I made was going to the NIH. I learned to do science, really learned to do science. The combination of Harvard and NIH. NIH was kind of the icing on the cake. I felt that I had been well prepared to be an independent investigator when I left, when I decided to leave NIH to go to Howard, because by then it had been almost ten years. I had been just at the bench doing nothing but research. I had no teaching responsibilities, no administrative responsibilities, no committees. Nobody asked me anything except about science.

I felt that I knew the people in the field. I always made it my business to get to know the movers and shakers so they would know who I am. I want to say how important networking is. It is so important. Knowing people is important. It is important to be good, to know your trade, but it is also important to be known by people who can help and mentor you. If you convince people that you are serious about your profession, that you are smart, that you will work hard, then they will support you. I always wanted to be known by the right people so I would go up to meet people—very famous people—and introduce myself, "I am Ken Olden, I work with Ira Pastan, and I work on this." When I was at Harvard I would do that as well.

By the time I left NIH to go to Howard University Cancer Center (HUCC), I was ready to do something that I always wanted to do. I started out at saying that I always wanted to make a difference. I wanted to go back to a historical black college or university and demonstrate to the world, not just to myself and African Americans, but could demonstrate to people like Ira Pastan and Eugene Kennedy at Harvard that there was nothing inferior about a black college. If you go there and you set high standards, and work hard, you can be as successful at doing research at Howard University as you can at NIH or Harvard.

Now there are barriers of course. You can't ignore the barriers but I thought that I could circumvent them and so it was time to give back. I knew how to write a grant and I knew people respected my work. If I went back and did what I had done at Harvard and NIH I would be funded. I could lead the development of a program to get peer review funding. I wanted to do that in a black institution. Howard offered me the chance to come there and do it. I decided to go over, first as scientific director, and I did that for about four and a half or five years, and then I was promoted to director of the HUCC.

JG: How did your colleagues at NIH, in the Laboratory of Molecular Biology, see that move?

KO: My colleagues at the NIH were very supportive. However, many of my friends outside of the NIH thought that it was not a good decision. That I should not do that.

JG: Why?

KO: Well, because they thought it was going to be a one-way ticket. In other words, I was going to go to Howard, I was not going to be successful, and then nobody wants a failure. NIH would not take me back because I would have been unproductive for four or five years. I made the decision though, and I knew myself, that I was going to go to Howard and I was going to work hard as I had become accustomed to at NIH and Harvard, and if there were barriers that I could not overcome, I was going to reach the conclusion within a year or two and come back to the NIH. Ira had enough confidence in me and he knew I was kind of waffling—should I do this or should I not—and Ira was one of the persons who helped me make the decision to do it.

He said Ken I know you and I know this is something you have always wanted to do. If I were you I would do it. I was tenured then, Ira recommended me for promotion to tenure, so I had a tenured position. He said I will hold your position for one or two years for you. You should take a leave of absence. I did not have to resign my tenured position. I took a leave of absence; he did not have to do that. It was something that he knew I wanted to do and he was my mentor. He wanted to promote my career. He wanted me to do what I wanted to do and he was a good friend. That is what he said and he did that. He kept my position until it was clear that I was going to be successful at Howard and I was not going to come back into the position. Ira served on the advisory board of the HUCC so he knew exactly what issues I faced at Howard and how I was doing.

I got the first three grant applications I submitted. I began to hire good people and continued to publish. My publication record went up not down. He knew that at any point I wanted to leave Howard I could leave. I made a commitment to myself that I was going to keep myself in a position so that if I wanted to go back to a Research 1 university I could do so. My track record was, my visibility, my credibility, it was just as good at Howard as it was at NIH.

As a matter of fact, *The Chronicle of Higher Education*, or some magazine of that caliber, conducted a study of scientists at black institutions. They did not know whether you were black or white, or whatever, but they concluded that I was number two out of one hundred in terms of number of publications and I was one out of one hundred in terms of citation impact. There was one fellow who had published many more papers than I had but he ranked sixty or seventy by citation impact. I was number two in the number of papers and I was number one in terms of citation impact. My publications were highly cited by others, my impact factor was high. I had lots of offers to leave Howard and I took the one to become Director of the National Institute of Environmental Health Sciences (NIEHS) at the NIH.

JG: You returned to NIH in 1991. How had NIH changed in those ten years? What was it like to return?

KO: NIH is in my estimation the premier research institution. If you want to do research, and that is what you want to do with your life, NIH is the best place in the world. There is just no better place than the NIH in terms of resources—intellectual and physical resources. They have money, they have equipment, they have what you need. If you can think of the right experiment to do you can do it at the NIH. Bright people want to work there; bright people do work there. I was very happy to get back to the NIH because I had spent now eleven and a half years at Howard and I succeeded in doing what I wanted to do. I wanted to take on a different challenge and I wanted to come back to NIH.

If anything, NIH has gotten better. I stayed in touch with the NIH and I followed the transition. I felt it was a top notch institution and it got even better during my time at Howard. There was an increased emphasis on scientific rigor and we began to hire. Although NIH made it a requirement that for every position that was available, we had to do a national/international search. You just could not promote somebody from within and there was a rigorous review process every four years. You could look at the people who were internal, but they had to apply for the position and they had to compete with others from all over the world. That is what Harold instituted at the NIH overall when he came. That was the new standard.

NIH was everything that I remembered it as being. It is a place that had very high standards and very good people and outstanding resources, and so I was not at all surprised or disappointed. I went back to Harvard in 2006 through 2007 and it was the same place it was when I was there in the 1970s. It still is committed to being the best and that is what NIH wants and is. That is the kind of environment that I wanted to be in.

JG: As we end up today speak about your responsibilities to the younger researchers. How do you help younger scientists move up through the profession?

KO: Right. I think by transmitting what I learned in my career and that is do ask important questions. If you are successful in answering them you will have an impact. Often people come along and they think about numbers of publications and that is necessary. You need to generate publications, but do something important. I encourage my postdocs always to ask and answer important questions and don't be afraid to be out front.

I will give just one example. When we decided to get into metastasis Ken Yamada and I made a decision about the first set of experiments we were going to do in metastasis. We decided to go after the critical issue in metastasis, and that is, can you prevent it. If you could prevent metastasis, you really would have a cure for cancer. We did not piddle around with this step or that step we asked how can you design a therapy an approach to prevent metastasis? We thought, based on our work with fibronectin, that you could do that, and Ken Yamada, independent of me, had demonstrated that there was a peptide sequence responsible for the binding to a receptor on the cell surface. There was a sequence of five amino acids referred to as GRGDS that represented the cell-binding domain of fibronectin. It was later shown by others that only three of these amino acids (RGD) was required for binding of fibronectin to the integrin receptor.

We thought we could use the peptide corresponding to the cell-binding domain to prevent metastasis. We designed an experiment to do just that, and we were able to block metastasis of some cell lines, most notably, melanoma which metastasize to the lung, and we were able to do this very successfully in a mouse model. This turned out to be another very, very highly cited and important paper that we published in *Science*. We were the first to demonstrate that one could block metastasis using anti-adhesive peptides. Now others came along after us, and did similar experiments using other anti-adhesive peptides. Our studies provided proof of principle that if you block adhesion of cells to extracellular matrix proteins like fibronectin and laminin you can prevent metastasis.

It turns out that you could block metastasis in an experimental animal model, but in humans, it did not work out so well. We spent a lot of time defining steps involved in the metastatic cascade and published many papers, but at some point you have to go after the jugular. Since cell adhesion is critical for metastasis, it follows that inhibiting cell adhesion should prevent metastasis. Therefore, we decided to use the approach to develop a therapy. I am still engaged in this area of research, and we have a very interesting paper coming out in the *Journal of Biological Chemistry* later this year.

It turns out that adhesion was not as simple as we thought it was in the 1970s and 1980s. It turns out that when extracellular matrix proteins bind to a receptor on the cell membrane, the interaction between the matrix protein and the receptor initiates a signaling cascade across the membrane. The protein signaling is what is really important and that is what we are now targeting to develop an effective drug therapy. That is what we are working on today. We hope to be able to identify a key signaling event.

I try to transmit my enthusiasm for science and my approach to young investigators. I would guess my biggest contribution has been in serving as a mentor, getting people into science as director of the NIEHS. I recruited personally many, many postdocs to come not only to NIEHS but to the NIH to do postdocs and to expose them to exciting research. I brought a lot of people to the NIH for the summer programs, undergraduates to expose them to the research world, not only research, but to the medical practice, so they could decide whether they wanted to be a physician or a physician scientist or a scientist with a Ph.D. I want people to know what the options are and what their life can be like if they choose one path versus the other.

In fact, I had an e-mail from somebody from NIEHS, I have not answered it, about a postdoc now and I am still going to do that because I have a lot of friends and contacts. If I meet someone who wants an experience in research, I can pick up the phone and call somebody at the NIH or Harvard or wherever and probably open a door, and I still do that.

JG: You mentioned that when you began your career that there were not a lot of mentors for you.

KO: Right.

JG: Do you think that the sciences are now color blind?

KO: No. It probably is no more now than it was when I came through, but the point is I never let that bother me. However, there were always people who will help you and I have had lots of mentors, but they have all been Caucasian males. Ira Pastan, Eugene Kennedy, and Bernard Davis were mentors. I am sure that racism was a barrier for me but I overcame the barriers because I am aggressive, I am ambitious. A lot of African Americans, Hispanics, Native Americans, do not feel comfortable being the only one, being the first, and I did not feel comfortable either but I made myself do whatever was necessary to succeed.

JG: Others might be turned away?

KO: They might be turned away and often it is not what is said but what one sees. If one lectures at the University of Tennessee or the University of Chicago every day and don't see anybody who looks like them or from their background this is a subtle statement that people like you don't make it in this profession for some reason. It is not relevant to you and your community. There are all of these subtle statements and this is what I meant when I said that I wanted to become a physician when I was in high school. I did not see blacks doing other things so I thought that meant you can't because you are not going to be allowed to.

When I was director of the NIEHS, African American students, Hispanics, and Native Americans, would come and talk to me because they look at me and say "Wow, he looks like me. He made it. He is probably going to be receptive to talking to me." Other directors would have been receptive too but there was that visual barrier. I would use my race to my advantage when I was standing out. I would go up to say hello to people and after a while they would know me even though I was an upstart. Very famous scientists would say after the third time: "Oh, yes, Ken Olden, I know who you are." Of course, I was the only black coming up to say hello to them, year after year at a major scientific conference. They began to associate my name, my face, my color with Ken Olden. I could use this opportunity to make an impression on this person.

I say to people now even if you are uncomfortable at social gatherings, as the only African American in the room, you still have, to go. People *don't* go out of their way to welcome you, you have to walk in and learn to talk to people, to have a conversation outside of science. You have to be comfortably enough to go up and say hello and break into a conversation and become part of the social fabric. I don't let any barrier, prevent me from doing what I need to do to get ahead.

I am now on a committee down in Washington, D.C., to advise policy makers on the use of science in decision making for the government. The committee is co-chaired by a former member of Congress and the former President of Stanford University. We had dinner last week before a meeting and I was the only African American in the room and I had to walk in and meet people, most of whom I did not know, and participate in the conversation and be part of the group. That is just what you have to do. A lot of people are not comfortable in those kinds of settings and they would rather go into professions like medicine where they are going to be other people that look like them and have the same cultural and social background.

I think the numbers though are bad. We still do not have enough people that you could walk in a room and expect to see two of you. I think that is a disadvantage in getting minorities to go into the field. I mean here at City University of New York there are one or two here and there. If you would come here, I think you would conclude that public health is not the field I want to go into because underrepresented minorities, are not represented. Maybe public health is not important to us. Science is important to us and it sends the wrong statement. You can be successful. I don't think there are any barriers that are not there for everybody. I have not had to overcome any barriers that a white person has not had to overcome. I had to work like everybody else, but no harder and no less.

JG: What about life-work balance for a scientist? You spoke about working weekends at the LMB. How do you balance both your professional and family obligations?

KO: That is a huge challenge irrespective of what your field is. I think it is for you, in your business, a historian there is always more work to do than there is time to do it, and Americans are becoming workaholics actually. You look at law, business, medicine, social sciences, no matter, the people who get to the top usually work long hours and there is the issue of balance. I think we all make decisions about that and you live with them because . . . I have four children and so I have made those kinds of decisions and I would say that I have not spent as much time with my children growing up as I wanted to, and I missed that and I've talked to them about that. They are adults now and they understand that. They were able, unlike me, to go to Vassar College, Haverford College, and have had great experiences that I did not have because I did what I did.

JG: Did any of them go into the sciences?

KO: No, not yet. I still have one young daughter who is in Hampton University. She is a junior and she is a pre-med major and she has thus far been doing very well in the sciences, so she wants to go to medical school after next year. Other than that, no. I have a son, an MBA in business, one in music, and a daughter in journalism. They did not go into science and I suspect in large part they saw a life that wasn't glamorous to them.

JG: You were appointed founding dean of the School of Public Health at Hunter College.

KO: Yes.

JG: It plans to open as an accredited school in 2011

KO: We have already opened. We have taken the first class of DPH. We have had a master's degree program for many years, but we are upgrading to a School of Public Health to provide training for the DPH. We are going to graduate the first person with a doctorate in Public Health in 2011. The hope is we will get fully accredited. You have to graduate at least one person before you can . . . That is required as a part of the application, so you have to graduate at least one DPH before you can become fully accredited. We hope to become fully accredited in 2011. That is what I came here to do and I have committed to two or three years.

JG: What do you do in the evenings? Any hobbies or reading?

KO: Yes. I just had lunch with a friend, back in North Carolina over the weekend and we talked about that. He is now retired and he was a scientist. He and I are both intellectuals. We like learning still and we are reading all kinds of things now and traveling and doing things. We were reading books about economics and business. I began a few years ago reading about different governments and how we got into this economic mess that we find ourselves now.

When Barack Obama started talking about change, I was talking about change with my friends before that, because you could see the handwriting on the wall. We have to change as a country otherwise we are going to go off the cliff. I read and I live theater. In the last month or so I have been to three performances. I like traveling. I am a wine connoisseur and I like preparing dinner for friends. I cook and I like to have friends over for dinner and wine. I like people. I put in twelve hours a day in the office, but when I go home and I usually don't take work home with me. I go home and I get a *New York Times* and *USA Today* and read those, watch the news, and then read a good book. Barnes and Noble is nearby. At this point in my life I wanted to grow and develop my interests in areas other than science.

JG: Last question. If you had one piece of advice, one lesson learned that you would like to pass onto a future scientist operating ten or twenty years into the future what would it be?

KO: I would advise them to pick important problems to work on. That has been the story of my life and it has made all the difference in the world. I always wanted to do things that would stand out. That would get attention. Not for egotistical reasons but because if you want to make a difference you just have so many years here on this earth. You have got to make sure that people who are in decision making and policy positions take notice of you and your ideas.

I write a lot of commentaries. I am just finishing up a commentary that I think is going to be accepted to the *New England Journal of Medicine*, and it is on an issue that I am interested in—health disparities. I think I understand what the issues are and I am trying to communicate that to youngsters and to the next generation of researchers and to current policy makers. I hope that I am visible enough that if I submit an article to the *New England Journal of Medicine*, and it gets published, that people will read it and it will influence. It is a way of influencing a large number of people, not just my friends, and my inner circle. If I publish in the *New England Journal of Medicine* and it gets through peer review, that says that people think this is an intelligent approach to a major national/international problem.

I constantly do that. I try to give a lot of thought to various public health or social problems and take a leadership role in doing something important. That is why I am serving on a Science Advisory Committee to advise the government on how to use science in decision making. This is something that the Bush administration is accused of devaluing. There are always two sides so how do you decide what science to use and what is good science and what is bad science? These are not easy decisions because some of these judgments are political or they are value-laden. I would also advise youngsters to get involved. Get involved, and whatever it is that turns you on, get involved and do it. No matter what you want to do, you can't have an impact unless you get involved. There are risks in getting involved, and you have to get out of your comfort zone, but just get involved in life. We need that.

JG: Dr. Olden, thank you very much.

KO: Well, thank you. Let me say I have the greatest admiration for Ira Pastan and he remains a mentor to me and he has been a good friend and he is the person that I think has done an outstanding job in training people that have gone off and they have been successful on their own. A lot of people train. You can go through some laboratories and get a lot of publications, but often when those people leave the lab they are not independent—they are not thinkers. Some people trained a hundred people but you can't name one or two that accomplished anything. Ira is different from that. If you take a look at the people who trained with Ira, they are out there someplace doing things that are important. All of them are doing very well and he should be very proud of them.

JG: Thank you very much.

KO: All right. I enjoyed talking with you.

JG: And you as well.

[End of Interview]